## REMARKS

This document is submitted in response to the Office Action dated February 24, 2006 ("Office Action"). Claims 27, 58, and 60 have been amended. Claims 28 and 61 have been canceled. Claims 22-26 and 30-57 were previously withdrawn.

Support for the amendments to claims 27, 58, and 60 is found in the Specification, e.g., at page 2, lines 2-11; page 3, lines 19-22; page 5, lines 17-26; page 5, lines 28-31; page 19, lines 12-15; page 24, line 29 through page 25, line 6; page 41, line 23 through page 44, line 17; and page 47, line 16 through page 50, line 21. No new matter has been introduced.

Upon entry of the proposed amendments, claims 27, 29, 58-60, and 62-64 will be under examination. Reconsideration of the application is respectfully requested in view of the remarks below.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 61 was rejected as lacking written description. See page 2, lines 10-11. As Applicants have canceled claim 61, the rejection of this claim is now moot.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 27-29, 58, 59, 61, 63, and 64 were rejected as indefinite. See page 3, lines 20-22. Applicants have canceled claims 28 and 61. Thus, their rejection is moot. Applicants address the grounds for rejection of the remaining claims as follows.

Previously presented claim 27, drawn to a method for producing stabilized denatured lipoprotein, recites (1) freezing a solution containing lipoprotein to produce a frozen solution of lipoprotein; (2) melting the frozen solution to produce a melted solution of denatured and stabilized protein; and (3) freeze-drying the melted solution to produce the denatured and stabilized lipoprotein in powder form.

The Office Action points out that while the claim implies that the act of freezing and melting a lipoprotein solution stabilizes it, the Specification does not support this process as being sufficient to stabilize the lipoprotein. See page 4, lines 8-10. It further notes that the Specification teaches that it is the freeze-drying step that stabilizes the lipoprotein. See the Office Action, page 4, lines 10-15.

Claim 27, as amended, does not recite a solution containing a stabilized denatured lipoprotein, i.e., the limitation objected to by the Office Action. Thus, Applicants respectfully submit that amended claim 27, as well as claims 29, 58, 59, 63, and 64 dependent from it, is definite.

Rejections under 35 U.S.C. § 102(b)

Claims 27 and 28 were rejected as being anticipated by U.S. Patent No. 4,749,522 to Kamarei ("Kamarei"). See page 6, lines 8-9. As noted above, claim 28 was canceled.

The Office Action notes that Kamarei discloses a method for extracting biomolecules including, *inter alia*, lipoprotein. It further notes that Kamarei discloses a number of pre-extraction steps including, *inter alia*, freeze-thawing and freeze-drying, which can be used in any combination. See page 6, lines 10-22. On this basis it concludes that claim 27 is anticipated.

Applicants would like to point out that claim 27, as amended, is drawn to a method for producing a stabilized denatured lipoprotein standard, which requires the additional step of determining an amount of the denatured lipoprotein in the powder. This step is nowhere disclosed in Kamarei. Thus, as Kamarei does not disclose all of the limitations of amended claim 27, Applicants respectfully submit that amended claim 27 is not anticipated by Kamarei.

Claims 27-29, 59, 60, and 62-64 were rejected as being anticipated by U.S. Patent No. 5,547,873 to Magneson *et al.* ("Magneson"). See page 7, lines 15-16.

In particular, the Office Action concludes that Magneson discloses a method for preparing stabilized proteins that includes all the steps recited in claim 27. See page 7, line 17 through page 8, line 3. Applicants respectfully disagree.

Amended claim 27 is drawn to a method for producing stabilized **denatured** lipoprotein. In contrast, Magneson states:

> This invention relates to a blood plasma or plasma-derived composition containing lipoproteins and other cardiovascular markers in a quality control material, which has been stabilized for long term dry storage and to recover essentially all of their native protein structural determinants ... In particular, this invention pertains to a freeze dry lyophilized human serum-based calibrator/control material that stabilizes its endogenous and exogenous lipoprotein and cardiovascular proteins' structural integrity for long term shelf life." (column 2, lines 9-19; emphases added)

Thus, Magneson clearly does not teach a method for producing a stabilized denatured lipoprotein. On the contrary, the method of Magneson is specifically directed to stabilizing lipoproteins in their native state as evidenced by the just-quoted passage.

In view of the foregoing remarks, it is respectfully submitted that amended claim 27, as well as claims 29, 59, 62, and 63 dependent from it, is not anticipated by Kamarei or Magneson. For at least the same reasons amended claim 60, as well as claim 64 dependent from it, is also not anticipated by these two references.

Rejections under 35 U.S.C. § 103(a)

Claims 58 and 61 were rejected as being obvious over Magneson in view of U.S. Patent No. 4,216,117 to Proksch *et al.* ("Proksch"). See page 9, lines 9-10. Claim 61 has been canceled. Thus, Applicants will only address the ground for rejection applicable to amended claim 58.

Amended claim 58, dependent from amended claim 27, is drawn to a method for producing a stabilized denatured lipoprotein standard as described above for claim 27, but in addition it includes adding a stabilizing agent to the frozen lipoprotein solution after melting, i.e., after the lipoprotein has been denatured by freezing.

The Office Action states that Magneson teaches the step of adding a stabilizing agent to a lipoprotein solution prior to lyophilization. However, it notes that Magneson does not teach addition of a stabilizing agent prior to a freezing step. See page 9, lines 11-16. It notes that Proksch, however, does disclose the step of adding a cryoprotective agent to the lipoprotein solution prior to freezing a lipoprotein solution. See page 9, lines 17-18. The Office Action alleges that "[s]ince the references teach in combination that optical clarity is achieved regardless of the order in which the sugars [stabilizing agents] are added and the lipoproteins are frozen, it would have been obvious to one of ordinary skill in the art to recognize that Proksch *et al.* provides an obvious equivalence to the method of Magneson *et al.* with respect to the order [of] adding a sugar to a solution of lipoprotein." See page 10, lines 8-12.

Applicants note again that, unlike the method covered by claim 58, the method of Magneson, as discussed above, is drawn to preparation of lipoprotein in a stabilized native state. Proksch discloses the addition of cryoprotective agents to a lipoprotein solution prior to freezing.

See column 4, lines 50-54. Applicants submit that addition of a cryoprotective agent to a solution of lipoprotein containing native protein prior to freezing, as disclosed by Proksch, prevents the lipoprotein from denaturing (i.e., it "cryoprotects" the lipoprotein). In contrast, the method recited in amended claim 58 requires denaturation of the lipoprotein. Consistent with this requirement, amended claim 58, unlike the teaching of Proksch, recites the addition of a stabilizing agent following melting of a lipoprotein solution, i.e., after freezing of the protein has already resulted in denaturation of the lipoprotein.

In sum, neither Magneson nor Proksch suggest a method for producing a stabilized, denatured, lipoprotein standard as required by amended claim 58. It is respectfully submitted that amended claim 58 is not rendered obvious by Magneson or Proksch.

## CONCLUSION

Applicants submit that all of the pending claims are novel, non-obvious and meet the written description and definiteness requirements. Allowance by the Examiner is respectfully solicited.

No fee is believed due. Please apply any charges to deposit account 06 1050, referencing attorney docket 13273-002001.

Respectfully submitted,

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